

### Remarks

Claims 1, 4, 6 and 21 are amended herein. New claims 39-40 are added herein. Claims 4, 6 and 21 are amended to correct form. Support for the amendment of claim 1 can be found throughout the specification, such as on pages 46-51, see for example page 48. Support for the amendment of claim 21, and new claims 39-40, can be found throughout the specification, such as, but not limited to, page 41 and pages 46-51.

Following entry of this amendment, claims 1-4, 6, 8, 10-13 and 21-33 and 39-40 are pending and are under examination. Claims 24-33 are withdrawn from consideration as being drawn to a non-elected invention.

Applicants believe no new matter is added herein. Reconsideration of the subject application is respectfully requested.

#### Rejections under 35 U.S.C. § 112, first paragraph

Claims 1-4, 6, 8, 10-13 and 21-23 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled by the specification. The Office action acknowledges that DNA encoding the VL and VH-PE38 were deposited with the ATCC in accordance with the Budapest treaty. However, the Office action alleges that monoclonal antibody 8H9 itself is required to practice the claimed invention. Applicants respectfully disagree. However, solely to advance prosecution, the claims are amended herein to refer to specific heavy and light chains deposited in Accordance with the Budapest Treaty. The Office action acknowledges receipt of Form PCT/RO/134 and the ATCC Deposit receipts confirming that the nucleic acid molecules encoding the heavy and the light chain of 8H9 were deposited in accordance with the Budapest Treaty as Accession Nos. PTA-5560 and PTA-5561 respectively. In view of the Deposits, and the amendment of the claims, reconsideration and withdrawal of the rejection are respectfully requested.

Claims 6, 8 and 10-12 were rejected under 35 U.S.C. § 112, first paragraph as allegedly not being enabled by the specification. The Office action states that amendment of the claim 6 to recite

“comprises **the** amino acid sequence” in place of “comprises **an** amino acid sequence” will overcome the rejection. Claim is amended herein in accordance with the Examiner’s suggestion, rendering the rejection moot.

*Rejections under 35 U.S.C. § 103*

Claims 1-4, 6-8, 10-13 and 21-23 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Modak et al. (Cancer Res. 61: 4048-4054, 2001) in view of U.S. Patent No. 5,618,920 (Robinson et al.) and Reiter et al. (Biochemistry 33: 5451-5459, 1994) and U.S. Patent No. 5,530,101 (Queen et al.). Claims 1-3, 6-8, 10-12 and 21-23 were rejected under 35 U.S.C. § 103 (a) as allegedly being obvious over U.S. Published Patent Application No. 2002/102264 (Cheung[a]), in view of Robinson et al., Queen et al. and Reiter et al. Claims 1-3, 6-8, 10-12 and 21-23 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over U.S. Published Patent Application No. 2003/0103933 (Cheung [b]) in view of Robinson, Reiter et al. and Queen et al. Claims 1-3, 6-8, 10-12 and 21-23 are rejected under 35 U.S.C. § 103 (a) as allegedly being obvious over U.S. Published Patent Application No. 2005/0169932 A1 (Cheung[c]) in view of Robinson et al., Reiter et al., and Queen et al. Applicants respectfully disagree with these rejections.

The Office action alleges that although the Declaration of Dr. Pastan under 37 C.F.R. 1.132 on May 18, 2007 provides evidence of the superior properties of 8H9-PE38, “the evidence submitted does not provide any results beyond what one of ordinary skill in the art might have expected based on the teachings of the references” (see page 8 of the Office action). The Office action agrees that the toxicity of 8H9(ds)Fv-PE38 is less than the toxicity of 8H9(scFv)-PE38. However, the Office action asserts that the significance or practicality of why it is an unexpected finding, nor is there any evidence that supports a conclusion of non-obviousness. The Office action alleges (see page 9) that one of skill in the art would predict that the dsFv form would provide advantages over a scFv form as this “flows naturally” from teaching on unrelated antibodies. Applicants respectfully disagree.

Submitted herewith is the Second Declaration of Dr. Pastan under 37 C.F.R. § 1.132 (hereinafter “the Second Declaration”). The Second Declaration provides additional evidence documenting that one of skill in the art would not be able to predict that 8H9(dsFv)-PE38 would be less toxic than the scFv form. The Second Declaration describes the results obtained with another

dsFv-PE38 form of an antibody, namely SSIP(dsFv)-PE38. SSIP(dsFv)-PE38 binds mesothelin (another antigen expressed in cancer). SSIP(dsFv)-PE38 was toxic at all doses; this antibody caused dermatologic injury and inflammatory reactions. Severe toxicity was noted at 300 µg/kg and 1,000 µg/kg; one animal in each study group died at each of these doses. The scFv form of this antibody, SSIP(scFv)-PE38, was toxic in monkeys at a similar dose (500 µg/kg). Thus, one of skill in the art could not predict if a specific dsFv antibody will be toxic. Moreover, as demonstrated in the Second Declaration, one of skill in the art would predict that a dsFv form of an antibody would be as toxic (or more toxic) than the scFv form. Thus, one of skill in the art would predict that 8H9(dsFv)-PE38 would be toxic at doses similar to those used with SSIP(dsFv)-PE38 (the lack of toxicity at these doses is not predictable). In addition, one of skill in the art would not predict that the 8H9(dsFv)-PE38 would be less cytotoxic than 8H9(scFv)-PE38. The results obtained with 8H9(dsFv)-PE38 were unexpected and simply could not be predicted from the cited prior art.

In view of the Declarations documenting the unexpectedly superior results obtained with the dsFv form of 8H9, reconsideration and withdrawal of the rejections under 35 U.S.C. § 103 are respectfully requested.

*Obviousness-Type Double Patenting*

Claims 1-3, 6-8, 10-13 and 21-23 were rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-2, 4, 6-7, 9, 11 and 52-54 of U.S. Patent Application No. 10/097,558 or in view of Reiter et al.

Applicants respectfully disagree with these rejections. The Declarations document the non-obvious nature of the presently claimed subject matter.

U.S. Patent Application No. 10/097,558 has not been allowed. Thus, Applicants request that these rejections be held in abeyance until the time that subject matter is considered to be allowable. A double-patenting rejection is premature if at least one of the patent applications has not been allowed or a patent issued. The Office action appears to indicate that U.S. Applicant No. 10/097,558 and the present application are commonly owned. However, the ownership of these applications is different, as the present application is jointly assigned.

*Request for Interview and Conclusion*

The prior response included a written request for an interview. However, the Examiner did not contact the undersigned representative to arrange a telephone interview. If any additional rejection is asserted, or if the present rejections are maintained, the Examiner is formally requested to contact the undersigned prior to issuance of the next Office action, in order to arrange a telephonic interview.

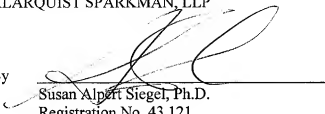
*This request is being submitted under MPEP §713.01, which indicates that an interview may be arranged in advance by a written request.* It is respectfully submitted that the present claims are in a condition for allowance, which action is requested.

Respectfully submitted,

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